UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,545	01/12/2004	David Phillips	048501/273281	1302

826 7590 06/04/2007

ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
06/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/755,545	PHILLIPS ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *8-12, 14-20 and 23-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: 1) NBCI Sequence entry for accession number NP_005851; 2) accession number XP_003891.

DETAILED ACTION

Election/Restrictions

Applicants' elections with traverse of Group I, claims 1-7, 13, 21 and 22, drawn to a pharmaceutical composition comprising follistatin, and of the species liver fibrosis in the reply filed on 09 March 2007 is acknowledged.

In said reply, Applicants "request that the Examiner reconsider the restriction between Groups I and XIX and/or Groups I-XVIII and XIX. Groups I-XVIII are drawn to pharmaceutical compositions comprising activin antagonists. Group XIX is drawn to a method of preparing pharmaceutical compositions comprising the activin antagonist...The Examiner argues that the claims in Group XIX (drawn to a method of making a pharmaceutical composition comprising an activin antagonist) can be 'used to produce a plurality of activin antagonists that are not recited by the instant claims [Groups I or Group I-XVIII]' (page 7, lines 12-14 of the September 14, 2006 Restriction Requirement). However, contrary to this assertion, claim 1 is a generic linking claim that recites a pharmaceutical composition comprising an activin antagonist, while the claims of Group XIX recite method of making an activin antagonist. It therefore is unclear what plurality of activin antagonist are not recited in the claims of Group I. The Examiner has failed to establish that the claims of Groups I and XIX and/or Groups I-XVIII and XIX are distinct."

Applicants' arguments have been fully considered and are not found persuasive. To clarify the Examiner's position, the product of claim 1 is generic to a plurality of

species of activin antagonists. Some of the species are claimed in the dependent claims; however, independent claim 1 still encompasses species that have not been specifically claimed. Similarly, the method of claim 23 is generic to a plurality of species that are both claimed and unclaimed. Thus, Applicants claimed species do not constitute an exhaustive list of activin antagonists.

Accordingly, the restriction requirement of 14 September 2006 set forth that Groups I-XVIII, were each drawn to separate pharmaceutical compositions comprising: follistatin (Group I), activin A antibody (Group II), activin AB antibody (Group III), activin B antibody (Group IV), antibody to dimer of inhibin β_A (Group V), antibody to dimer of inhibin β_B (Group VI), ActRIIA antibody (Group VII), ActRIIB antibody (Group VIII), ActRIA antibody (Group IX), ActRIB antibody (Group X), ALK2 antibody (Group XI), ALK4 antibody (Group XI), activin A receptor antibody (Group XIII), activin AB receptor antibody (Group XIV), activin B receptor antibody (Group XV), Smad6 (Group XVI), Smad7 (Group XVII), and TGFβ/activin type I receptor inhibitor (Group XVIII).

As stated previously, Inventions XIX and each of I-XVIII and XXII are related as process of making and product(s) made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the process as claimed can be used to produce a plurality of activin antagonists that are not recited by the instant claims. For example, claim 23 encompasses preparing a pharmaceutical composition comprising a dominant negative SMad3 protein, for

example, (which is one of the plurality of activin antagonists not recited by the claims). However, in addition, the products as claimed are distinct because the products of Groups I-XVIII can be made by another and materially different process, i.e., the compositions of said Groups can be prepared in methods that do not require homogenously mixing the activin antagonist with a pharmaceutically acceptable carrier, adjuvant, and/or diluent (as required by the process of Groups XIX).

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-12, 14-20 and 23-49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in the reply filed on 09 March 2007.

Claims 1-7, 13, 21 and 22 are under consideration to the extent that said claims read on the elected invention, i.e., a pharmaceutical composition comprising follistatin. It is also acknowledged that claim 1 is a linking claim for some of the instantly pending claims.

Sequence compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 for the following reasons. The instant specification and claims

contain sequences, which are not properly identified and therefore are not in compliance with 37 C.F.R. § 1.821(d).

In response to the instant office action, Applicants must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). For example, claims 3, 4 and 7 are drawn to proteins identified by accession number or by amino acid length, etc. Instead, the proteins must have a reference point which would be a protein identified by sequence identifier number (SEQ ID NO:) in each of the claims.

In addition, the instant specification will need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to a particular amino acid or nucleic acid sequence. Applicants must provide a computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). See M.P.E.P. 2420-2435.

Applicants are advised to review the entire text of the instant specification for compliance with sequence rules.

Applicants' cooperation is requested in correcting any other sequence references in the specification or claims that do not include a sequence identifier.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 30 August 2004 is enclosed in this action.

Claim Objections

Claim 5 is objected to because of the following informalities: the claimed Markush group recited the word "and" twice (see line 4). Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 13, 21 and 22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,470,826. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to follistatin proteins and pharmaceutical compositions.

Claims 1-7, 13, 21 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 87 of copending Application No. 10/318,283. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 87 of the '283 application is drawn to a pharmaceutical composition comprising an activin inhibitory molecule.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-7, 13, 21 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 60 of copending Application No. 10/575,049. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 60 of the '049 application is drawn to a pharmaceutical composition comprising an activin modulatory molecule.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-7, 13, 21 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 51 and 57-60 of copending Application No. 10/571,837. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '837 application are drawn to pharmaceutical compositions comprising follistatin isoforms/analogues.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 13, 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1-7, 13, 21 and 22 are directed to pharmaceutical compositions comprising a protein and optionally a pharmaceutically acceptable carrier, adjuvant and/or diluent. It is unclear how a pharmaceutical composition only optionally contains a pharmaceutically acceptable carrier, adjuvant and/or diluent.

Claim 4 recites that the follistatin protein is a single chain protein classified as NCBI protein XP_003891, AAH040107. However, XP_003891 has been removed from the database (see attached NBCI Sequence entry for accession number XP_003891). Thus, it is unclear what protein is encompassed by claim 4.

Claim 5 recites that the composition exists in a form selected from the group consisting of: follistatin/chelate, follistatin/drug, follistatin/prodrug, follistatin/toxin, follistatin/detector group and follistatin/imaging marker. It is unclear what each member of the instant Markush group encompasses. For example, it is unclear whether follistatin/drug refers to a follistatin composition having follistatin as the only active ingredient or to a follistatin composition having an additional active ingredient (an additional drug).

Appropriate corrections are required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, 7, 13, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Bartholin et al. (Oncogene. 2001 Sep 6;20(39):5409-19).

The claims are directed to a pharmaceutical composition comprising follistatin, or a fragment or analogue thereof.

Accordingly, the Bartholin et al. reference teaches the follistatin-related protein (or follistatin analogue) as defined in Genebank accession number NP_005851(see also attached NBCI Sequence entry for accession number NP_005851), thus meeting the limitations of claims 1, 2, 6, 7, 21 and 22. The Bartholin et al. reference also teaches that the protein binds to and antagonizes activin (p.5409, col.2), thus meeting the limitations of claim 13. It is noted that claim 1 and dependent claims do not require a pharmaceutically acceptable carrier, adjuvant and/or diluent, as these are optional. It is also noted that the limitations of "a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate" in claim1, of "wherein the disease associated with fibrosis is one of: a hyperproliferative or inflammatory fibrotic disease; a pulmonary fibrosis; an inflammatory bowel disease, or a related condition such as ulcerative colitis or Crohn's Disease; or liver fibrosis or cirrhosis" in claim 21, and of "wherein the disease associated with fibrosis is liver fibrosis or cirrhosis" in claim

22 are directed to the preamble of claim 1 and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of the claimed compositions. Regardless, the follistatin composition of the Bartholin et al. reference is not incompatible with a therapeutic intention.

Since the reference teaches all the elements of the claims, claims 1, 2, 6, 7, 13, 21 and 22 are anticipated by Bartholin et al.

Claims 1, 2, 3, 5, 13, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,041,538 to Ling et al.

The claims are directed to a pharmaceutical composition comprising follistatin, or a fragment or analogue thereof.

Accordingly, the '538 patent teaches pharmaceutical compositions comprising follistatin combined with a pharmaceutically acceptable carrier (col.10, lines 1-3), thus meeting the limitations of claims 1, 2, 5, 13, 21 and 22. Although the '538 patent does not appreciate that the follistatin protein binds to and antagonizes activin, this is nonetheless an inherent property of said protein. Applicants are reminded that chemical compounds and their properties are inseparable (In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA1963)), as are their processes and yields (In re Von Schickh, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). Thus, the reference meets the limitations of claim 13. It is again noted that the limitations of "a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate" in

claim1, of "wherein the disease associated with fibrosis is one of: a hyperproliferative or inflammatory fibrotic disease; a pulmonary fibrosis; an inflammatory bowel disease, or a related condition such as ulcerative colitis or Crohn's Disease; or liver fibrosis or cirrhosis" in claim 21, and of "wherein the disease associated with fibrosis is liver fibrosis or cirrhosis" in claim 22 are directed to the preamble of claim 1 and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of the claimed compositions.

In addition, the '538 patent teaches that the follistatin proteins of the invention (follistatin A, which has 315 amino acids and follistatin B, which has 288 amino acids) are single chains, have molecular weights of approximately 35,000 Daltons and 32,000 Daltons, respectively (as estimated by SDS-PAGE), were isolated from follicular fluid and are able to inhibit FSH (col.1, lines 20-24 and 40-68, col.7, lines 11-14 and 64), thus meeting the limitations of claim 3.

Since the reference teaches all the elements of the claims, claims 1-5, 13, 21 and 22 are anticipated by U.S. Patent No. 5,041,538 to Ling et al.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is 571-272-8149. The examiner can normally be reached Monday through Friday from 9:00AM to 5:30PM (EST) .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
25 May 2007

ELIZABETH C. KEMMERER, PH.D.
PRIMARY EXAMINER